Chapter 4

Depressive and anxious mood after stroke

Abstract

Aims of the present study were describe the level and course of anxious and depressive mood from three to fifteen months post-stroke and to evaluate the effects of neurological variables, demographic factors, disabilities and life events on mood at fifteen months post-stroke. Mood was divided into late life and post-stroke mood by attribution of patients themselves. A group of 101 first-ever ischemic stroke patients was assessed at three and fifteen months post-stroke using self-report questionnaires. A control group consisting of 70 elderly subjects was also assessed with the same time interval. The results showed that late life anxious and depressive mood remained constant from three to fifteen months post-stroke, whereas post-stroke mood improved significantly. While disabilities not related to stroke were associated with late life mood, post-stroke disabilities were associated with post-stroke mood. Psychosocial disabilities best predicted post-stroke anxious and depressive mood at fifteen months post-stroke. For post-stroke anxiety, the experience of life events and younger age were also predictive of higher anxiety at follow-up.

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Introduction

Post-stroke and late life depression

Estimates of the prevalence of major depression are 10 to 15 percent within the first few months after stroke in a community-based population (Burvill et al., 1995, House et al., 1991). Minor depression has been diagnosed in an additional 8 to 14 percent of community-dwelling stroke patients (Burvill et al., 1995, Pohjasvaara et al., 1998). The course of depression after stroke remains unclear as some researchers reported little diagnosable depression after one year (House et al., 1991), whether others mentioned one third of patients developing depressive symptoms within the first year after stroke (Herrmann et al., 1998). For several years, researchers have investigated the nature of depression after stroke, but have not reached similar conclusions (Aben et al., 2001). While some researchers stress the importance of neurological factors in post-stroke depression, others consider it primarily to be a psychological reaction to the consequences of stroke (Robinson et al., 1994; Gainotti et al., 1999). Recently, one recognizes that there is no definite evidence to accept or refute a solely neurological or psychological mechanism in the occurrence of depression following stroke (Whyte & Mulsant, 2002). Depression after stroke is multifactorial and might be regarded within a biopsychosocial model or stress-vulnerability model. (Oldehinkel et al., 2003, Whyte & Mulsant, 2002).

Neurological factors that have been associated with depression after stroke include stroke severity, vascular risk factors and silent brain infarctions (Dennis et al., 2000, Alexopoulos et al., 1997, Fujikawa et al., 1993). A relationship between depressive symptoms and lesion location has not been consistently demonstrated and seems, in part, dependent on the time of measurement since stroke onset (Carson et al., 2000, Robinson et al., 1984). Variables which can be viewed in terms of vulnerability are increasing age, female sex or psychiatric disorder prior to stroke (Dennis et al., 2000, Burvill et al.,1995, Herrmann et al., 1998). Stressors or psychosocial risk factors that have been found to influence depression after stroke were functional disability and other life events that occurred after stroke. (Bisschop et al., 2004, Singh et al., 2000, Herrmann et al., 1998, Bush, 1999, Burvill et al., 1997).

Some factors associated with post-stroke depression, have also been related to depression in a group of elderly people without brain damage. Prevalences of late life depression in a population based study lay around 15 percent (Schoevers et al., 2003a,

Beekman et al., 2001). Recent studies showed older age, female gender, marital status, stressful life events and a history of anxiety or depression to be related to a higher incidence of depression in late life (Schoevers at al., 2003a, Schoevers at al., 2003b, Oldehinkel et al., 2003, Beekman et al., 2001; Palsson et al. 2001). Also, a mutual relationship between disability and depression has been established in both clinical and community dwelling elderly (Lenze et al., 2001).

Post-stroke and late life anxiety

In comparison to studies on depression, little studies have investigated anxiety after stroke, although in both stroke patients and elderly subjects without brain damage, the presence of depression is often associated with the presence of anxiety (Lenze et al., 2001; Castillo et al., 1995). A community-based stroke study showed that anxiety as measured with the Hospital Anxiety and Depression scale (HADS) occurred in 23 percent of patients 4 months post-stroke (Johnson et al., 1995). While physical disability is often found to be related to depression, a less strong relationship seems to exists between disability and anxiety after stroke (Dennis et al., 1999; Lenze et al., 2001). As for depression, a history of psychiatric disorders has also been related to the occurrence of early-onset anxiety after stroke (Castillo et al., 1995). The relationship between anxiety and lesion location has not been consistent across different studies (Castillo et al., 1993; Starkstein et al., 1990).

In studies on anxiety in community dwelling older persons, 10 percent of subjects scored above cut-off of the HADS anxiety scale, while 3 percent was diagnosed with generalized anxiety (Schoevers et al., 2003a, Beekman et al., 1998). In the few longitudinal studies that have been conducted on anxiety of elderly subjects, best predictors for becoming anxious were older age, being female and the occurrence of stressful life events, especially death of one's partner (Schoevers et al., 2003a, de Beurs et al., 2000).

Aims of present study

To sum up, depressive and anxious mood are quite prevalent among older persons and raise to affect approximately one third of community-dwelling subjects after a stroke. Depression and anxiety often co-occur after stroke and are influenced by multiple factors, of which some can be viewed in terms of vulnerability and others as stress-inducing factors. Several of these factors related to post-stroke depression and anxiety seem to be the same as those found to affect late life depression and anxiety. In the

present study, the level and course of depressive and anxious mood of stroke patients will be compared to mood of age-matched controls. An attempt is made to distinguish post-stroke depression from late life depression by asking stroke patients themselves if their mood can be attributed to the stroke event. Furthermore, the predictive value of several factors for late life and post-stroke depressive and anxious at fifteen months post-stroke will be analysed. Vulnerability factors included are age, gender, marital status and lesion characteristics. In addition, the impact of physical and psychosocial disabilities and stressful life events after stroke will be investigated, the presence of which might induce stress.

Methods

Stroke patients

To obtain a sample not solely biased by admission to hospital or rehabilitation centres, 235 stroke subjects were recruited through the aid of 100 general practitioners (GPs) from the northern part of the Netherlands and the stroke unit of the University Hospital Groningen. All subjects approved of the fact that their medical history was provided by the GP. At T1, 122 patients met inclusion criteria and were willing and able to participate, while 101 patients could be included at T2. See Chapter 1 for a detailed prescription of patient exclusion and drop-out. Mean age of these patients was 65.4 (SD=11.9) at the start of the study, ranging from 32 to 93 years. The group consisted of 64 men and 37 women. Of these patients, 90 lived independently, 4 semi-independently and 7 lived in a nursing home. At T1, medication was recorded of 85 patients of whom 12 used sedative and 10 used antidepressive medication. At T2, medication as prescribed by the GP was collected of 99 patients. Sedative medication was now used by 9 patients and antidepressive medication by 10 patients. Non-participation at T2 was related to higher late life depression scores at T1. Patients who did and who did not participate at T2 did not differ in anxiety scores at T1.

Control subjects

Control subjects were recruited among the population of four general practices from the northern part of the Netherlands. A stratified randomisation procedure was used to match the control subjects to patients on age and gender. Control subjects with a history of psychiatric disturbances, neurological conditions or alcohol abuse were

excluded from the study. At T1 80 control subjects were interviewed. It appeared afterwards that one subject had suffered previous neurological damage, another subject had a history of psychiatric disturbances. Both were excluded from the study. At T2, the control group consisted of 70 subjects, 8 subjects had dropped out because they did not want to participate again (n=4), were too busy (n=2) or had moved (n=2). The level of anxious or depressive mood at T1 did not affect the participation at T2. Mean age of the control subjects at the start of the study was 66.9 (SD=11.9) which did not differ significantly from the age of the stroke subjects (t=0.8, p=.42). Within the control group, 39 men and 31 women participated, the ratio of gender did not differ significantly from the patient group (X^2 =1.0, p=.32). Neither did the percentage of subjects with or without a partner differ between patients and control subjects (79 % vs. 74 % with partner, X^2=0.6, p=.45). Mean level of education was also comparable between patients and control subjects (Z=-0.2, p=.82). Next, control subjects did not differ from stroke patients in the use of antidepressive or sedative medication at T1 or T2 (T1, sedatives X^2=0.3, p=.62; antidepressants X^2=2.8, p=.10; T2 sedatives X^2=0.4, p=.55; antidepressants X^2=1.4, p=.24)

Lesion characteristics

Classification of the side of ischemic damage was based on neurological data. Of 91 patients CT-scan findings were present, mean time between onset of stroke and CT-scan was 10 days (SD=36 days) with a range of 0 to 291 days. On the basis of all neurological data, lateralization of lesion of 98 patient could be classified: 41 had right-sided damage, 48 left-sided damage, 4 bilateral lesions and 5 had lesions affecting brain stem or cerebellum. As has been well documented, a stroke can be preceded by transient ischemic attacks or silent brain infarctions. In our study, one third of CT-scans of patients demonstrated one or more silent infarctions of the brain, localised either unilaterally or bilaterally. To be able to analyse the effect of silent brain infarctions on mood, patients are divided into three groups a) subjects with no silent brain infarctions, b) subjects with one silent brain infarction and c) subject with multiple silent brain infarctions.

Procedure and Measures

All subjects were assessed twice at their own place of residence by trained interviewers with an interval of approximately one year. After signing an informed consent, several questionnaires concerning functional ability, mood, changes in emotion and cognition

and quality of life were administered. Only those instruments relevant for the current research question will be described.

Depression and anxiety

The Hospital Anxiety and Depression Scale (HADS) was used to measure anxious and depressive mood (Zigmond & Snaith, 1983). The HADS has an anxiety and a depression sub-scale both containing 7 items (scored 0 to 21). Higher scores indicate a greater likelihood of anxiety or depression. According to Johnson et al. (1995), when examining a community based stroke group, best cut-off scores for the HADS are 5 for the depression scale and 6 for the anxiety scale. Following de Beurs et al. (2000), when measuring change in HADS scores from T1 to T2, only scores who exceed the cut-off and have changed with 3 or more scale points are considered to be changed reliably. Both sub-scales of the HADS correlate highly, although principal component analysis demonstrated a two factor solution for the HADS in several studies (Johnson et al., 1995; Spinhoven et al., 1997).

In the present study, after a confirmative answer on an item of the HADS, stroke patients were asked if they attributed the depressive or anxious mood questioned in this item to the stroke event. Total anxiety and depression scores can thus both be divided into a stroke related score, the addition of scores attributed to the stroke event, and into a total of scores not attributed to the stroke event. Both stroke related and non-stroke related scores are divided by the number of items to obtain a mean score. The non-stroke related depression and anxiety of stroke patients and the depression and anxiety of control subjects will be further referred to as respectively late life depression and late life anxiety.

Physical and psychosocial disabilities

The Stroke Adapted –Sickness Impact Profile (SA-SIP) is a 30-item stroke-adapted version of the original SIP (van Straten et al., 1997; Bergner et al., 1981). The SA-SIP measures functional health status on 8 subscales. All items are scored 'yes' (1) or 'no' (0); scores range from 0-30 with higher scores indicating poorer functional health. Principal component analysis has shown that a physical dimension can be formed by the scales Body care and movement, Mobility, Household management and Ambulation. A psychosocial dimension can be formed by the scales Social Interaction, Communication, Emotional Behaviour and Alertness Behaviour. Internal reliability proved to be

high for both the physical scale (alpha=.82) and the psychosocial scale (alpha=.78) (van Straten, 1997). In the present study, after each item of the SA-SIP, stroke patients were asked if the disability is seen as a consequence of stroke. All items on which impairment is attributed to stroke were summed, as well as the items that were not related to stroke.

Life events

The Social Readjustment Rating Scale was adapted to assess the number and impact of life events experienced within the year between measurements (Holmes & Rahe, 1967). Only the ten items ranked most highly on their estimated influence on life changes were presented to the stroke patients and the control subjects. Next, subjects could report other life events that were not covered by these ten items. Subjects could indicate how they experienced the impact of the life event with scores ranging from (0) none to (5) very much. Both the number of life events and their impact scores were calculated to overall scores. When examining the effect of separate life events, only those events reported by at least 10 percent of subjects will be analysed.

Statistical analysis

Mood of stroke patients and control subjects was compared by using independent samples T-tests. Chi-square analyses were used to compare the number of patients and controls scoring above depression and anxiety cut-offs. To measure change in the level of mood from T1 to T2, paired samples T-tests were performed, while changes in cut-off scores were analysed using Mc Nemar's test for two dichotomous related variables.

The evaluation of factors predictive of mood at T2 was performed in two steps. First the association between demographic variables, physical and psychosocial disabilities and life events on the one hand and late life and post-stroke mood on the other was evaluated by investigating correlations and by comparing means. Next, the combined predictive value of the investigated variables was analysed using the GLM univariate procedure. Continuous predictor variables were entered into the regression model as covariates, while dichotomous variables were entered as fixed factors. All statistical analyses were performed in SPSS 9.0.

Results

Late life and post-stroke anxiety and depression for stroke patients and control subjects at T1 and T2

Investigation of correlations
At T1, 75 percent of depression scores and 64 percent of anxiety scores of stroke patients were attributed to the stroke event. At T2, patients attributed 67 percent of depression scores and 50 percent of anxiety scores to the stroke.

For control subjects, at both times of measurement, depression scores were significantly related to anxiety scores (T1, r=.48, p=.00; T2 r=.42, p=.00). For stroke patients, post-stroke depression scores correlated significantly with post-stroke anxiety scores (T1 r=.52, p=.00; T2 r=.42, p=.00) as was also the case for late life depression and anxiety scores (T1 r=.26, p=.01; T2 r=.22, p=.03). There were no significant correlations between post-stroke anxiety scores and late life anxiety (T1 r=.04, p=.69; T2 r=.05, p=.59) or between both depression scores (T1, r=-.19, p=.06; T2 r=-.11 p=.29).

Comparison of anxiety and depression scores between patients and controls
Comparison of the total HADS anxiety scores of stroke patients and control subjects at T1 and T2 showed that anxiety scores did not differ significantly between the two groups (T1, Stroke: M=2.7, SD=3.1, Control: M=2.0, SD=3.0 t=-1.6, p =.11; T2, Stroke: M=2.0, SD=2.7, Control: M=1.4, SD=2.3, t=-1.5, p=.13). Comparison of late life anxiety scores also showed no significant differences between the two groups at T1 and T2 (T1: t=1.2, p=.22; T2: t=0.6, p=.57). Total depression scores were significantly higher for patients than controls at both times of measurement (T1, Stroke: M=3.4, SD=3.2, Control: M=1.1, SD=1.5,t =-6.3, p=.000; T2, Stroke: M=2.5, SD=3.3, Control: M=1.4, SD=2.0, t=-2.7, p=.008). Further analysis showed that late life depression scores did not differ significantly between the two groups (T1, t=0.1, p=.96; T2, t=1.5, p=.13).

Impact of lesion characteristics on late life and post-stroke anxiety and depression
When comparing unilateral right and left hemisphere stroke patients at T1 and T2, neither post-stroke nor late life mood scores differed between the two groups (Late life anxiety: T1, t=0.2, p=.82; T2, t=0.1, p= .91; Post-stroke anxiety: T1, t=0.7, p=.50; T2, t=0.1,

p=.93; Late life depression: T1, t=-0.3, p=.76; T2, t=1.9, p=.07; Post-stroke depression: T1, t=-0.1, p=.92; T2, t=-1.0, p=.34). The presence of silent brain infarctions also did not significantly affect late life or post-stroke mood at three or fifteen months post-stroke (Late life anxiety: T1, F=1.3, p=.29; T2, F=2.7, p=.07; Post-stroke anxiety: T1, F=0.5, p=.60; T2, F=1.5, p=.23; Late life depression: T1, F=0.4, p=.67; T2, F=2.1, p=.13; Post-stroke depression: T1, F=0.2, p=.81; T2, F=1.8, p=.17).

Course of anxiety and depression scores

Figure 1 and Table 1 show that post-stroke depression and anxiety improved significantly from T1 to T2. For both patients and controls, late life anxiety and depression remained at the same level between T1 and T2.

GLM Repeated Measures analyses showed significant improvement from T1 to T2 in post-stroke anxiety (Time, F=16.4, p=.000, Time*Side, F=0.6, p=.43) and post-stroke depression (Time, F=10.7, p=.002, Time*Side, F=0.5, p=.50) for both right hemisphere and left hemisphere stroke patients. Furthermore, the presence of silent brain infarctions did not affect the course of post-stroke depression (Time*SBI, F=1.2, p=.28) or post-stroke anxiety scores (Time*SBI, F=.07, p=.80).

Figure 1. Course of mean late life (LL) and post-stroke anxiety and depression scores from T1 to T2 for stroke patients and control subjects.

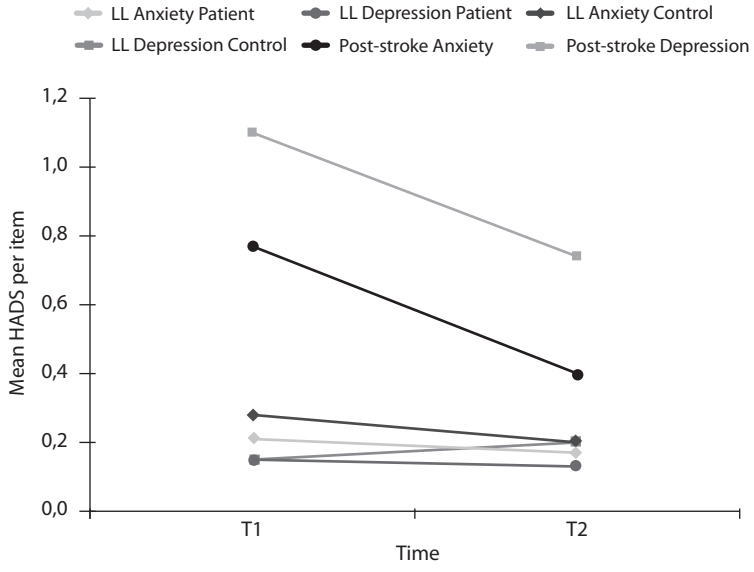

Table 1. Paired-samples t-test of post-stroke and late life anxiety and depression between T1 and T2 for patients (n=100) and control subjects (n=70).
*** p <.05; ** p < .01, *** p <.001 (two-tailed)**

HADS scores	Patient T1 M (SD)	Patient T2 M (SD)	Paired t-value	Control T1 M (SD)	Control T2 M (SD)	Paired t-value
Late Life Depression	0.2 (0.3)	0.1 (0.3)	0.5	0.2 (0.2)	0.2 (0.3)	-1.9
Post-stroke Depression	1.1 (1.0)	0.7 (0.8)	3.8***			
Late Life Anxiety	0.2 (0.4)	0.2 (0.3)	1.1	0.3 (0.4)	0.2 (0.3)	2.0
Post-stroke Anxiety	0.8 (0.9)	0.4 (0.7)	4.8***			

Prevalences of total anxiety and depression

As Table 2 presents, at both times of measurement, significantly more patients scored above depression cut-off than controls. Patients did not differ from controls, however, in the proportion of subjects scoring above anxiety cut-off or in the number of new anxiety or depression cases. Unilateral right and left hemisphere stroke patients did not differ in the number of subjects scoring above cut-off at T1 or T2 for anxiety or depression.

Table 2. Number and percentages of patients (n=100) and control subjects (n=70) scoring above HADS depression and anxiety cut-off at T1 and T2 and number and percentages of subjects scoring above HADS depression and anxiety cut-off at T2, but not at T1 (new cases).
*** p < .05, ** p < .005, *** p < .001 (two-tailed)**

	T1			T2			New cases		
	Stroke n (%)	Control n (%)	X^2	Stroke n (%)	Control n (%)	X^2	Stroke n (%)	Control n (%)	X^2
HADS dep	28 (28)	3 (4)	16.2***	17 (17)	3 (4)	6.4 *	6 (6)	2 (3)	0.9
HADS anx	14 (14)	7 (10)	0.6	12 (12)	5 (7)	1.1	5 (5)	2 (3)	0.5

At T1, 8 patients (29% of depressed cases and 57% of anxious cases) were both anxious and depressed, at T2 this occurred in 7 patients (41% of depressed cases, 58% of anxious cases). In the control group, 1 subject was both depressed and anxious at T1 and T2. Statistical analyses showed significantly less depression cases on T2 compared to T1 for patients, but not for controls. Anxiety cases did not differ significantly from T1 to T2 for both patients and controls.

Factors related to late life and post-stroke depression and anxiety at T2

Age

In the control group, age was positively related to depression scores (r=.35, p=.003) but not to anxiety scores (r=-.00, p=.95). For stroke patients, there was a small, nonsignificant, relation between age and late life depression scores at T2 (r=.16, p=.11). There appeared to be no significant relation between age of the patients and post-stroke depression scores (r=.11, p=.30). Age of the patients, however, correlated negatively with post-stroke anxiety scores, indicating greater anxiety among younger stroke patients (r=-.28, p=.005). No relationship was present between age and late life anxiety for stroke patients (r=-.07, p=.52).

Gender

Male control subjects did not differ from female subjects on depression or anxiety scores at T2 (Depression: Male, M=1.0, SD=1.4; Female, M=1.7, SD=2.5, t=-1.3, p=.20, Anxiety: Male, M=1.5, SD=2.2, Female, M=1.4, SD=2.5, t= 0.1, p=.94). In the stroke group, gender had neither an effect on mean post-stroke depression scores nor on mean post-stroke anxiety scores (Depression: Male, M=0.8, SD=0.9; Female, M=0.6, SD=0.7, t=0.9, p=.37, Anxiety: Male, M=0.4, SD=0.7, Female, M=0.4, SD=0.8, t=0.3 , p=.78). Female stroke patients, however, had significantly higher mean late life anxiety scores than male stroke patients (Depression: Male, M=0.1, SD=0.2; Female, M=0.2, SD=0.3, t=-1.2, p=.22, Anxiety: Male, M=0.1 SD=0.2 , Female, M=0.3, SD=0.4, t=-2.4, p=.02).

Marital status

The presence of a partner did not seem to affect mood at the second time of measurement, although depression scores tended to be somewhat higher for both control subjects and stroke patients who did not have a partner compared to subjects with partner (Controls: M=2.0, SD=2.4 vs M=1.1, SD=1.8, t=-1.7, p=.09, Patients: M=1.4, SD=2.7 vs M=0.7, SD=1.3, t=-1.3, p=.21).

Physical and psychosocial disabilities

At T2, physical and psychosocial disability scores were higher for patients than for controls. (Physical disability: M=4.4, SD=4.3 vs M=1.5, SD=2.2, t=-5.7, p=.00; Psychosocial disabilities: M=3.7, SD=3.2 vs M=1.5, SD=2.3, t=-5.3, p=.00).

Table 3 shows correlations between non stroke related and post-stroke physical and psychosocial disabilities at T2 and late life and post-stroke mood at T2. In the control group, a significant relationship was found between physical disabilities and psychosocial disabilities on the one hand and depression and anxiety scores on the other. For stroke patients as well, a significant relationship was found between psychosocial disabilities not related to stroke and late life depression and anxiety. Physical disabilities not related to stroke were, however, only significantly associated with late life depression but not with late life anxiety. Post-stroke physical and psychosocial disabilities were significantly related to both post-stroke depression and post-stroke anxiety.

Table 3. Bivariate Pearson's correlations between late life and post-stroke mood and non stroke related (NS-) and post-stroke (PS-) physical (PHYS) and psychosocial (PSYCHO) disabilities for patients (n =100) and control subjects (n=70) at T2.
*** p <.05; ** p <.01; *** p <.001 (two-tailed)**

	Control		Patient			
	PHYS	PSYCHO	NSPHYS	NSPSYCHO	PSPHYS	PSPSYCHO
Late Life Depression	.52***	.37**	.40***	.27**	-.10	-.13
Post-stroke Depression			.02	.10	.46***	.47***
Late Life Anxiety	.26*	.30*	-.01	.24*	.08	.11
Post-stroke Anxiety			-.18	.03	.34**	.51***

Life events

Patients (n=82) and controls (n=70) retrospectively reported a mean of one life event within the previous year. The mean impact of life events did not differ between patient and control group (M=2.4 vs M=3.0, Z=-.8, p=.41). The most frequently mentioned life event was 'death of a family member or friend', reported more often by control subjects (n=31) than by patients (n=22) (X^2=5.1, p=.02). This life event was also ranked most highly concerning the impact score. Eleven control subjects mentioned an illness of themselves within the last year and 21 patients mentioned an illness other than the stroke within the year after stroke (X^2=2.2, p=.14). The third frequent life event was 'illness of a family member', reported by 17 control subjects and 15 stroke patients (X^2=0.8, p=.37). Table 4 shows that life events within the previous year were significantly related to late life anxiety for control subjects, but to post-stroke anxiety for stroke patients. In stroke patients, the impact of personal illness was related to higher post-stroke anxiety (rs=.32, p=.004). Within the control group, no relationship was found between the impact of individual life events and mood.

Table 4. Spearman's correlations between number and impact of Life events (LE) and late life depression (LLDEP), post-stroke depression (PSDEP), late life anxiety (LLANX) and post-stroke anxiety (PSANX) for control subjects (n=70) and stroke patients (n=82) at T2.
*** p <.05; ** p <.01; *** p <.001 (two-tailed)**

	Control		Patients			
	LLDEP	LLANX	LLDEP	PSDEP	LLANX	PSANX
Total number LE	.11	.22	.19	.13	.00	.32**
Total impact LE	.13	.31**	.21	.04	.06	.15

Multivariate prediction of late life and post-stroke anxiety

In correlational analyses, several factors were found to influence anxiety and depression in both control subjects and stroke patients at T2. All variables showing a significant relation to either anxiety or depression at T2 were entered into the General Linear Model. For late life depression and anxiety these included age, gender, non stroke related disabilities, and number and impact of life events. The same variables were used to predict post-stroke mood, except now post-stroke disabilities were entered as covariates.

Table 5. GLM multivariate prediction of late life (LLANX) and post-stroke anxiety (PSANX) in patient group and late life anxiety scores (LLANX) of control subjects at T2.

	Control		Patient			
	LLANX		LLANX		PSANX	
	F	p	F	p	F	p
Age	0.8	.38	0.1	.79	9.0	.00
Gender	0.3	.61	8.4	.00	0.1	.76
Post-stroke physical disabilities					1.0	.32
Post-stroke psychosocial disabilities					12.4	.00
Non stroke related physical disabilities	3.8	.06	2.1	.15		
Non stroke related psychosocial disabilities	1.3	.26	8.7	.00		
Total number of life events	1.6	.21	1.4	.25	3.8	.05
Total impact of life events	3.9	.05	1.1	.29	0.0	.85
Corrected model (including intercept)	2.6	.03	3.3	.00	9.8	.00

As Table 5 shows, 6 percent of the variance of anxiety in the control group could be explained by the impact of life events (Corrected model, R^2=.21). Gender predicted 10 percent of the variance of late life anxiety for stroke patients, while non-stroke related psychosocial disabilities explained another 11 percent (Corrected model, R^2=.21). For

post-stroke anxiety several predictors could be found among which impairments in psychosocial functioning after stroke had the greatest impact. Younger age and the experience of a greater number of life events also predicted worse anxiety scores at fifteen months post-stroke (Corrected model, R^2=.34).

Multivariate prediction of late life and post-stroke depression

Table 6 presents the outcome of the GLM analyses used to predict depression scores at T2. Within the control group, 12 percent of the variance of depression could be explained by physical disabilities. Age did not appear to explain variances in depression independently from disabilities (Corrected model, R^2=.34). Late life depression in stroke patients at T2 could not be predicted by the model used in the analyses (Corrected model, R^2=.14). Of post-stroke depression, 25 percent of variance could be explained by age of the patient and psychosocial disabilities after stroke, while physical disabilities did not appear to be an independent significant predictor (Corrected model, R^2=.34).

Table 6. GLM multivariate prediction of late life (LLDEP) and post-stroke depression (PSDEP) in patient group and late life depression scores (LLDEP) of control subjects at T2.

	Control LLDEP		Patient LLDEP		PSDEP	
	F	p	F	p	F	p
Age	1.5	.22	0.2	.63	4.5	.04
Gender	0.0	.89	0.0	.84	0.8	.38
Post-stroke physical disabilities					0.0	.98
Post-stroke psychosocial disabilities					17.1	.00
Non stroke related physical disabilities	8.3	.00	1.6	.21		
Non stroke related psychosocial disabilities	2.6	.11	1.1	.31		
Total number of life events	0.3	.62	0.0	.91	1.7	.20
Total impact of life events	0.7	.39	1.8	.18	1.5	.22
Corrected Model (including intercept)	5.3	.00	2.0	.08	6.3	.00

Discussion

Late life and post-stroke mood

In the present study, late life and post-stroke mood was distinguished by stroke patients themselves. This process of attribution of mood to different causes could, however, be distorted, for example by impairments in cognition or emotion after stroke. Also, the

emotional impact of the stroke event itself can bias patients to attribute all existing disturbances in mood to the impact of stroke. Besides, when both stroke-related and non stroke related factors affect mood in the same individual, it can be hard to disentangle the two. Despite these possible biases, several findings in the present study support the distinction between late life mood disturbances and post-stroke changes in mood based on the perception of patients. First, post-stroke mood was not related to late life mood. Second, the level of late life depression and anxiety did not differ between stroke patients and elderly control subjects without cerebral pathology. Moreover, in both groups, mean level of late life anxious and depressive mood did not change significantly over time. In contrast, post-stroke anxious and depressive mood improved between three and fifteen months post-stroke. Next, while disabilities not related to stroke were associated with late life mood, disabilities after stroke were associated with post-stroke mood.

Course of late life and post-stroke mood

An important aim of this study was to describe the course of mood between three and fifteen months post-stroke. During this time interval, 21 percent of patients dropped out. Non-participation of stroke patients was in part selective: it appeared to be related to a higher level of late life depression at three months post-stroke. Stroke patients lost from T1 to T2 were also older and physically more severely disabled than subjects who stayed in the study. The results therefore concern the less depressed, less disabled and somewhat younger stroke patients.

Between three and fifteen months post-stroke, the percentage of depressive stroke patients decreased significantly, but remained significantly higher than the percentage of control subjects scoring above cut-off. The depression cases in the stroke group, 28 percent at T1 and 17 percent at T2, are similar to other community based stroke studies (House et al., 1991; Johnson et al., 1995). Because of the relative low number of subjects who scored above cut-off, depression and anxiety cases have not been further divided into stroke related or non-stroke related, which can be interesting for studies using larger samples. The percentage of depressive control subjects (4%) is similar to another study on late life depression in the Netherlands (de Beurs et al., 2001), but is quite low. This might partly be caused by the exclusion of subjects who had gone through depressive episodes prior to participation in the study. The new incident depression cases, 6 percent for patients and 2 percent for control subjects are similar to those found in

the prospective study of Andersen and colleagues (1994). It is important to note that the incidence of new depression cases between three and fifteen months post-stroke did not differ from the incidence of new cases in elderly controls.

In both the stroke and control group, the level of anxiety was related to the level of depression. Analyses of double cases within the stroke group showed that anxiety was more strongly related to depression than vice versa. In contrast to depression, neither anxiety scores nor the number of anxious subjects differed between stroke patients and elderly control subjects. Also, the number of anxiety cases in the stroke group did not decrease between T1 and T2. The percentage of stroke patients scoring as anxious, 14 percent at three and 12 percent at fifteen months post-stroke, is quite low in comparison to another community based study (Johnson et al., 1995). Again, the selection criteria used in this study could be partly responsible for the relative low number of anxious patients. Stroke patients with previous psychiatric disorders were excluded, the occurrence of which has been related to early-onset anxiety after stroke. The proportion of elderly control subjects with anxiety scores above cut-off, 10 percent at T1 and 7 percent at T2, are in line with another study of community dwelling older persons (Beekman et al., 1998).

Prediction of late life and post-stroke mood

Another important aim of the present study was to evaluate the role of different contributing factors for late life and post-stroke depression and anxiety at fifteen months post-stroke. In the present study, only those patients and controls were included who were not diagnosed or treated for previous psychiatric disorders. It might be that in this group a different risk profile is related to the onset of depression or anxiety than in subjects with previous psychiatric disorders. Vulnerability and stress-inducing factors included in the present study were neurological factors, demographical variables, disability measures and stressful life events.

It appeared that late life depression in stroke patients could not be predicted adequately by the current model. Of post-stroke mood at fifteen months post-stroke, 25 to 30 percent of variance could be explained. This indicates that several other factors not included in this study mediate the occurrence of depression or anxiety. One of them could be personality characteristics such as neuroticism (de Beurs et al., 2001) or individual coping styles.

Multivariate prediction of late life and post-stroke anxiety

In stroke patients, the experience of psychosocial disabilities was predictive of both late life and post-stroke anxiety. As has also been found in previous research, physical disabilities were less strongly related to anxiety and did not emerge as a significant predictor for late life or post-stroke anxiety (Dennis et al., 2000). Besides psychosocial disabilities, female gender predicted higher late life anxiety in stroke patients, while younger stroke patients experienced greater post-stroke anxiety. These findings are in line with those from a study of anxiety up to two years after stroke (Schultz et al., 1997). An explanation for these findings might be that the impact of disabilities after stroke might be greater in younger stroke patients. Analyses of the cognitive functions of the present patient group, for example, showed that older stroke patients did not differ from the control subjects on a diversity of cognitive tasks, while stroke patients below the age of 65 were significantly more impaired than control subjects similar in age (Gerritsen, 2004). In the present study, psychosocial disabilities were not predictive of anxiety in the control group. Psychosocial disabilities include a diversity of cognitive, social and emotional disabilities, some of them specifically affected after stroke. They should be further analysed to gain insight into those factors that have greatest impact on anxiety after stroke.

In both patients and controls, a greater number or a higher impact of life events was related to a greater level of anxiety, but not to higher depression scores. Contrary to a recent longitudinal study in the Netherlands, individual stressful life events did not appear to be related to late life anxiety scores in elderly community dwelling subjects (de Beurs et al., 2001). Possibly, serious life events occurred too infrequently to be able to measure significant effects, for example only three control subjects reported the loss of one's partner. In stroke patients, however, the personal life event of illness to oneself was associated with anxiety after stroke. This is in line with the ideas of Finley-Jones and Brown (1981) who suggested that life events involving threat can lead to anxiety. The finding that individual threatful life events do relate to anxiety in stroke patients, contrary to control subjects, indicates that patients may have become more vulnerable after stroke.

Late life and post-stroke depression

In univariate analyses, the side of lesion and the presence of silent brain infarctions did not affect the level or course of mood after stroke. These findings fit with recent

reviews that could not find consistent replications concerning the impact of specific lesion sites on depressive mood after stroke (Carson et al., 2000, Whyte & Mulsant, 2002). Furthermore, in studies that did find an association between specific lesion locations and depression, the impact was quite small and seemed restricted to the acute phase after stroke (Whyte & Mulsant, 2002). In line with previous studies, physical disabilities appeared as most predictive for depression in elderly controls (Lenze et al., 2001). However, in stroke patients not physical but psychosocial disabilities after stroke most strongly predicted post-stroke depression. While older age was not associated with post-stroke depression in single correlational analysis, it emerged as a predictor in multivariate prediction. This last finding is most likely confounded by the association between older age and greater physical disabilities. A great number of previous studies have investigated the impact of physical disabilities on depression after stroke. The present study indicates that the broad range of psychosocial disabilities should also be subject of investigation.

A biopsychosocial model of post-stroke mood?

At first glance, the importance of the experience of psychosocial disabilities for post-stroke mood and the lack of influence of lesion characteristics seem to offer support for a psychological rather than a neurological model of mood in the chronic phase after stroke. However, extensive neuro-imaging data lacked for a part of the stroke patients, so a proper investigation of the impact of specific lesion sites on mood after stroke could not be performed. On the other hand, the association between psychosocial disabilities and mood does not preclude any effect of the lesion location on mood after stroke. Psychosocial disabilities include a diversity of cognitive, social and emotional disabilities which could be both a direct and an indirect effect of stroke. The present study showed that slightly different factors increased the vulnerability for post-stroke anxious and depressive mood. In addition to greater disabilities that predicted both post-stroke depressive and anxious mood, younger age and the experience of life events after the occurrence of a stroke influenced anxiety at fifteen months post-stroke.

References

Aben, I., Verhey, F., Honig, A., Lodder, J., Lousberg, R., & Maes, M. (2001). Research into the specificity of depression after stroke: a review on an unresolved issue. *Progress in Neuro-psychofarmacology and Biological Psychiatry, 25*, 671-689.

Alexopoulos, G., Meyers, B., & Young, R. (1997). Clinically defined vascular depression. *American Journal of Psychiatry, 154*, 562-565.

Andersen, G., Vestergaard, K., Riis, J., & Lauritzen, L. (1994). Incidence of post-stroke depression during the first year in a large unselected stroke population determined using a valid standardized rating scale. *Acta Psychiatrica Scandinavica, 90*, 190-195.

Beekman, A.T., Bremmer, M.A., Deeg, D.J., van Balkom, A.J., Smith, J.H., de Beurs, E., et al. (1998). Anxiety disorders in later life: a report from the Longitudinal Aging Study Amsterdam. *International Journal of Geriatric Psychiatry, 13*, 717-726.

Beekman, A.T., de Beurs, E., van Balkom, A.J.L.M., Deeg, D.J., van Dyck, R., & van Tilburg, W. (2000). Anxiety and depression in later life:co-occurrence and communality of risk factors. *American Journal of Psychiatry, 157*, 89-95.

Beekman, A.T., Deeg, D.J., Geerlings, S.W., Schoevers, R.A., Smit, J.H., & van Tilburg, W. (2001). Emergence and persistence of late life depression: a 3-year follow-up of the Longitudinal Aging Study Amsterdam. *Journal of Affective Disorders, 65* (2), 131-138.

Bergner, M., Bobbitt, R.A., Carter, W.B., & Gilson, B.S. (1981). The Sickness Impact Profile: development and final revision of a health status measure. *Medical Care, 19*, 787-805.

de Beurs, E., Beekman, A., Geerlings, S., Deeg, D., van Dyck, R., & van Tilburg, W. (2001). On becoming depressed or anxious in late life: similar vulnerability factors but different effects of stressful life events, *British Journal of Psychiatry, 179*, 426-431.

de Beurs, E., Beekman, A.F.T., Deeg, D.J.H., van Dyck, R., & van Tilburg, W. (2000). Predictors of change in anxiety symptoms of older persons: results from the Longitudinal Aging Study Amsterdam, *Psychological Medicine, 30*, 515-527.

Bisschop, M., Kriegsman, D.M.W., Deeg, D.J.H., Beekman, A.T.F., & van Tilburg, W. (2004). The longitudinal relation between chronic diseases and depression in older persons in the community: the Longitudinal Aging Study Amsterdam. *Journal of Clinical Epidemiology, 57*, 187-194.

Burvill, P., Johnson, G., Jamrozik, K., Anderson, C., Stewart-Wynne, E., & Chakera, T. (1995). Prevalence of depression after stroke: The Perth Community Stroke Study. *British Journal of Psychiatry, 166* (3), 320-327.

Burvill, P., Johnson, G., Jamrozik, K., Anderson, C., & Stewart-Wynne, E. (1997). Risk factors for post-stroke depression. *International Journal of Geriatric Psychiatry, 12*, 219-226.

Bush, B.A. (1999). Major life events as risk factors for post-stroke depression. *Brain injury, 13*, 131-137.

Carson, A., MacHale, S., Allen, K., Lawrie, S., Dennis, M., & House, A. (2000). Depression after stroke and lesion location: a systematic review. *Lancet, 356*, 122-126.

Castillo, C.S., Starkstein, S.E., Fedoroff, J.P., Price, T.R., & Robinson, R.G. (1993). Generalized anxiety disorder after stroke. *Journal of Nervous and Mental Diseases, 181* (2), 100-106.

Castillo, C.S., Schultz, S.K., & Robinson R.G. (1995). Clinical correlates of early-onset and late-onset post-stroke generalized anxiety. *American Journal of Psychiatry, 152*, 1174-1179.

Dennis, M., O'Rourke, S., Lewis, S., Sharpe, M., & Warlow, C. (2000). Emotional outcomes after stroke: factors associated with poor outcome. *Journal of Neurology, Neurosurgery and Psychiatry, 68,* 47-52.

Finley-Jones, R., & Brown, G.W. (1981). Types of stressful life event and the onset of anxiety and depressive disorders. *Psychological Medicine, 168*, 50-57.

Fujikawa, T., Yamawaki, S., & Touhouda, Y. (1993). Incidence of silent cerebral infarction in patients with major depression. *Stroke, 24*, 1631-1634.

Gerritsen, M.J.J. (2004). *Cognitive aftermath of ischemic stroke, a longitudinal community-based study* [dissertation]. University of Groningen.

Gainotti, G., Azzoni, A., & Marra, C. (1999). Frequency, phenomenology and anatomical-clinical correlates of major post-stroke depression. *British Journal of Psychiatry, 175*, 163-167.

Herrmann, N., Black, S.E., Lawrence, J., Szekely. C., & Szalai, J.P. (1998). The Sunnybrook stroke study. A prospective study of depressive symptoms and functional outcome. *Stroke, 29*, 618-624.

Holmes, T.H., & Rahe, R.H. (1967). The Social Readjustment Rating Scale. *Journal of Psychosomatic Research, 11*, 213-218.

House, A., Dennis, M., Mogridge, L., Warlow, C., Hawton, K., & Jones, L. (1991). Mood disorders in the first year after stroke. *British Journal of Psychiatry, 158*, 83-92.

Johnson, G., Burvill, P.W., Anderson, C.S., Jamrozik, K., Stewart-Wynne, E.G., & Chakera, T.M. (1995). Screening instruments for depression and anxiety following stroke: experience in the Perth community stroke study. *Acta Psychiatrica Scandinavica, 91*, 252-257.

Lenze, E.J., Mulsant, B.H., Shear, M.K., Alexopoulos, G.S., Frank, E., & Reynolds, C.F. (2001). Comorbidity of depression and anxiety disorders in later life. *Depression and Anxiety, 14*, 86-93

Oldehinkel, A.J., Ormel, J., Brilman, E.I., & van den Berg, M.D. (2003). Psychosocial and vascular risk factors of depression in later life. *Journal of affective disorders, 74*, 237-246.

Palsson, S.P., Ostling, S., & Skoog, I. (2001). The incidence of first-onset depression in a population followed from the age of 70 to 85. *Psychological Medicine, 31* (7), 1159-1168.

Pohjasvaara, T., Leppavuori, A., Siira, I., Vataja, R., Kaste, M., & Erkinjuntti, T. (1998). Frequency and clinical determinants of poststroke depression. *Stroke, 29* (11), 2311-2317.

Robinson, R.G., Kubos, K.L., Starr, L.B., Rao, K., & Price, T.R. (1984). Mood disorders in stroke patients. Importance of lesion location. *Brain, 107*, 81-93.

Schoevers, R.A., Beekman, A.T.F., Deeg, D.J.H., Jonker, C., & van Tilburg, W. (2003a). Comorbidity and risk-patterns of depression, generalised anxiety disorder and mixed anxiety-depression in later life: results from the AMSTEL study. *International Journal of Geriatric Psychiatry, 18*, 994-1001.

Schoevers, R.A., Beekman, A.T., Deeg, D.J., Hooijer, C., Jonker, C., & van Tilburg, W. (2003b). The natural history of late-life depression: results from the Amsterdam Study of the Elderly (AMSTEL). *Journal of affective disorders, 76*, 5-14.

Schultz, S.K., Castillo, C.S., Kosier, J.T., & Robinson, R.G. (1997). Generalized anxiety and depression. Assessment over 2 years after stroke. *American Journal of Geriatric Psychiatry, 5*, 229-237.

Shimoda, K., & Robinson, R.G. (1999). The relationship between poststroke depression and lesion location in long-term follow-up. *Biological Psychiatry, 45*, 187-192.

Singh, A., Black, S.E., Herrmann, N., Leibovitch, F.S., Ebert, P.L., Lawrence, J., & Szalai, J.P. (2000). Functional and neuroanatomical correlations in poststroke depression: the Sunnybrook Stroke Study. *Stroke, 31*, 637-644.

Spinhoven, P., Ormel, J., Sloekers, P.P., & Kempen, G.I. (1997). A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychological Medicine, 27*, 363-370.

Starkstein, S.E., Cohen, B.S., Fedoroff, P., Parikh, R.M., Price, T.R., & Robinson, R.G. (1990). Relationship between anxiety disorders and depressive disorders in patients with cerebrovascular injury. *Archives of General Psychiatry, 47* (3), 246-251.

van Straten, A., de Haan, R.J., Limburg, M., Schuling, J., Bossuyt, P.M., & van den Bos, G.A. (1997). A stroke-adapted 30-item version of the Sickness Impact Profile to assess quality of life (SA-SIP30). *Stroke, 28*, 2155-2161.

Whyte, E.M., & Mulsant, B.H. (2002). Post stroke depression: epidemiology, pathophysiology and biological treatment. *Biological Psychiatry, 52*, 253-264.

Zigmond, A.S., & Snaith, R.P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*, 361-370.